

As an initial matter, the Applicant confirms the election of Claims 1-10 and 16 drawn to an apparatus, and confirms that Claims 11-15 are withdrawn without prejudice to refilling.

In the Official Action, the only rejections were made on the basis of prior art references. However, the main reference cited by the Examiner, namely McPherson et al. 5,096,676, is the exact antithesis of the present invention which is directed to a protein crystallization tray that will ensure that when stacked, the lower portion of the upper tray does not directly impinge upon the top of the sealable wells in the tray below it. Accordingly, since the Examiner appears to have missed the central feature of the present invention, Applicant will provide more information concerning the invention and its background.

In particular, the invention relates to a protein crystallization tray which has sealable wells in which protein crystallization procedures take place, and in such procedures, a coverslip which may be made of thin glass is placed over the sealable well in order to allow the crystallization process to take place. In order to ensure that the well is properly sealed, a material which is typically silicon grease is placed around the outer edges of the cover slip which maintains the wells in sealed condition for the duration of the crystallization process. Neither the coverslip nor the silicon grease can be disturbed during the protein crystallization procedure, otherwise the particular crystallization process will be wasted and proper crystals will not form. The use of silicon grease on the glass coverslips has thus made it impossible to stack these trays because the lower portion of the protein crystallization tray will impinge upon the glass coverslip when the trays are stacked leading to two problems. First, when the silicon grease touches the bottom of the protein crystallization tray, it smears the bottom with silicon which is difficult if not

impossible to remove. In addition, it is more often the case that the glass coverslip when it contacts the bottom portion of the tray on top of it will stay in contact with the upper tray, and when the upper tray is pulled away from the tray below it, the coverslip will be removed from the protein crystallization well, and again the crystallization process in that well is irrevocably disrupted.

Accordingly, the present invention provides a protein crystallization tray which has been designed to allow protein crystallization processes to take place in wells sealable by a coverslip and silicon grease, and yet which can be stacked and unstacked without any disruption of the protein crystallization processes going on inside of the wells. The stacking of these trays, which has not been previously accomplished, provides a distinct advantage in that a large number of protein crystallizations can take place at one time under conditions suitable for such crystallizations to take place. The stackability of the trays of the present invention also is particularly advantageous when the protein crystallization processes are designed to be carried out in zero-gravity environments such as would be possible in vehicles in Earth's orbit wherein space is extremely limited. The stackable trays of the present invention thus maximize the number of crystallization events or experiments that can take place in such limited quarters.

With this in mind, it is clear that none of the prior art references cited by the Examiner, either singly or in combination, disclose or suggest the subject matter of the claimed invention. For example, as indicated above, the Examiner cited the McPherson US patent 5,096,676 when indeed this patent discloses the type of tray wherein the top part of the sealable well directly impinges upon the lower end of the tray or well above up, as is clearly shown in Fig. 6 of the McPherson patent. As shown in this Figure, the McPherson tray is clearly stacked so that the bottom part of upper tray is in direct contact

with the upper part of the well in the tray below it. In the McPherson tray, well 20 is covered by cover means 34 which is in the form of a sheet, but the sheet 34 over well 20 is directly impinged by the lower end of the tray on top of it. Moreover, although Figure 6 is described as an alternative embodiment, indeed the patent disclosure states that this "apparatus is identical to that previously described" except for the provision of porous plastic material placed in the solution wells. See Col. 5, lines 30-40. The McPherson tray thus would suffer the same problems that would arise if the wells were sealed with a glass coverslip and silicon grease as described above, and is thus the exact **opposite** of the present invention. Accordingly, McPherson clearly does not disclose or suggest the present invention, and in fact **teaches away** from the invention because it teaches a stacking system wherein the bottom portion of the upper tray or well directly contact the top of the well below it.

With this in mind, it is clear that no other reference cited by the Examiner, either singly or in combination, discloses or remotely suggests the subject matter of the claimed invention. For example, the Examiner also rejected the claims on the basis of the Turre US Patent 4,415,418. Once again, it is clear that Turre neither discloses or suggests the present invention in that, in the first place, the Turre patent does not relate to a device for achieving protein crystallization, but instead relates to a gel electrophoresis apparatus which is far different than the present tray. Moreover, the mechanism for stacking the tray in Turre actually impinges directly on the cover sheet below it and thus once again this reference does not disclose or suggest the present invention, but **teaches away** from it because the stacking means impinge directly on the cover sheet. In Turre, this is seen in that the "feet" 14 will be planted directly on cover sheet 13 which goes over the tray 1. Clearly, there is no teaching or suggestion in Turre of the present invention since not only

does Turre relate to a far different apparatus from the present invention, it teaches once again that the lower portion of the upper tray will end up on the coversheet over the top surface of the lower tray when stacked.

The Examiner also rejected Claim 6 on the combination of McPherson and Turre. This rejection is respectfully traversed in that for reasons as stated above, neither McPherson nor Turre, either singly or in combination, disclose or suggest the present invention as claimed in Applicant's present claim 1, and thus the dependent claims are patentable over these references for at least the same reasons as discussed above.

Finally, the Examiner rejected Claims 1-10 and 16 on the basis of the Applicant's prior reference, US patent 5,419,278, in view of the Miller US patent 5,384,103 or Tabler US patent 4,600,103. This rejection, insofar as applied to the claims as amended, is respectfully traversed since yet again, none of these references, either singly or in combination, discloses or suggests the essential features of the present invention, namely the provision of a stackable protein crystallization tray wherein the lower end of the crystallization well does not impinge upon the top of the sealable well in the tray below it. In the first place, the Examiner acknowledges that the Applicant's own prior patent, US 5,419,278, does not disclose or suggest the present invention, and indeed the present invention is an improvement over trays such as those disclosed in the earlier Carter patent wherein the problems with stacking crystallization trays were not recognized or addressed in any manner. The Examiner has attempted to overcome the lack of recognition of such a problem in Carter by citing to trays which have nothing whatsoever to do with the types of trays need for protein crystallization, and thus the references cited by the Examiner, Miller and Tabler, clearly do not disclose or suggest a solution to the particular problem solved by the present invention and thus cannot be combined with

Carter to make obvious the present claims. The Miller reference merely relates to a medical tray with feet for stacking, and indeed these stacking feet can enter circular apertures 90, 92, 94 and 96 such that the bottom of the upper tray can impinge upon the bottom of the lower tray. There is clearly no disclosure or suggestion in Miller of a tray wherein the bottom has to be away from the top of the upper tray which is not surprising since Miller relates to a general medical tray and **not** to a tray for protein crystallography wherein the upper wells need to be adequately sealed with a coverslip and silicon grease. Accordingly, the Miller reference cannot be added to the Carter patent to disclose or suggest the present invention.

Moreover, having exhausted any disclosure in a field which might be even remotely equated with the field of protein crystallography, the Examiner's cited Tabler reference is taken from the bakery field and merely shows a stackable tray for baked goods. Suffice it to say that the Applicant concedes that stackable trays are known in the art in many unrelated fields such as the baking industry, but is not remotely understood how the Examiner is making the jump from a tray used with baked goods such as cakes to a tray that must meet all the requirements of a protein crystallization tray with individual wells that must be sealed in a particular manner so that a protein crystallization process would take place. Indeed, there is no disclosure or remote suggestion in Tabler that would address the present situation wherein the bottom of a particular crystallization well needs to be kept from contact with the top of the tray below it. Accordingly, there is clearly no disclosure or suggestion in a reference dealing with bakery products which would be remotely applicable to Applicant's present stackable protein crystallization tray, and thus it is clear that the Tabler reference to a bakery basket cannot be combined with Carter to make obvious Applicant's present claims to a stackable crystallization tray.

Accordingly, it is clear that none of the cited references, either singly or in combination, disclose or suggest the invention as presently claimed, and the Examiner's rejections on the basis of the cited prior art are respectfully traversed and should be withdrawn.

In light of the amendments and arguments as set forth above, Applicant submits that the present application is now in condition for immediate allowance, and such action is earnestly solicited.

Respectfully submitted,



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ATTACHMENT A

Amendments to the Claims

Following herewith is a complete listing of the claims, including a marked copy of the currently amended claims.

1. (currently amended) An apparatus for carrying out a protein crystallization process~~suitable for use in carrying out a chemical or biological process~~ comprising:
a stackable tray containing at least one sealable well in which a protein crystallization process~~chemical or biological process~~ may be performed, said tray having an upper surface substantially coplanar with an upper opening in said sealable well and sealable with a coverslip, and side walls extending beyond the lowermost surface of said sealable well, said side walls having a lower end configuration so as to form an outer base capable of allowing said tray to be stacked on the outer portion of the upper surface of a second stackable tray positioned below the first tray while maintaining separation between the upper openings of the second stackable tray and the lower surface of the sealable wells of the first stackable tray so as to allow stacking of said trays without a lid to prevent impingement of the upper well openings by the lower surface of the first tray.
- 2-4. (canceled).
5. (original) The apparatus of claim 1 wherein said sealable well is sealable with clear plastic tape.
6. (original) The apparatus of claim 1 further comprising an automated system for stacking and unstacking said stackable trays.

7. (currently amended) The apparatus of claim 21 wherein the protein crystallization process comprises a hanging-drop vapor-equilibration method.

8. (original) The apparatus of claim 1 wherein the tray is comprised of a material selected from the group consisting of plastic and glass.

9. (original) The apparatus of claim 1 further comprising a solution capable of forming crystals within said well.

10. (original) The apparatus of claim 1 further comprising a second stackable tray stacked below said first tray.

11-15. (withdrawn).

16. (currently amended) An apparatus suitable for use in growing protein crystals, said apparatus comprising: a stackable tray containing at least one sealable well for performing a protein crystallization process, said tray having an upper surface substantially coplanar with an upper opening in said sealable well, said well being capable of being sealed using a coverslip, and side walls extending beyond a lower surface of said sealable well, said side walls having a lower end configured so as to allow said tray to be stacked on top of another stackable tray with said lower surface of said sealable well disposed at a position raised above said upper surface of the other tray stacked below thereby allowing stacking of the trays without the lowermost surface of the wells of the upper tray contacting the upper openings of the wells of the tray below it.